Volume Conduction Effects on Wavelet Cross-Bicoherence Analysis

IRFAN ALI MEMON*, MUHAMMAD SIDDIQUE KALHORO, AND NIZAMUDDIN CHANNA*****

RECEIVED ON 26.08.2012 ACCEPTED ON 18.09.2012

ABSTRACT

Cross-bicoherence analysis is one of the important nonlinear signal processing tools which is used to measure quadratic phase coupling between frequencies of two different time series. It is frequently used in the diagnosis of various cognitive and neurological disorders in EEG (Electroencephalography) analysis. Volume conduction effects of various uncorrelated sources present in the brain can produce biased estimates into the estimated values of cross-bicoherence function. Previous studies have discussed volume conduction effects on coherence function which is used to measure linear relationship between EEG signals in terms of their phase and amplitude. However, volume conduction effect on cross-bicoherence analysis which is quite a different technique has not been investigated up to now to the best of our knowledge.

This study is divided into two major parts, the first part deals with the investigation of VCUS (Volume Conduction effects due to Uncorrelated Sources) characteristics on EEG-cross-bicoherence analysis. The simulated EEG data due to uncorrelated sources present in the brain was used in this part of study. The next part of study is based upon investigating the effects of VCUS on the statistical analysis of results of EEG-based cross-bicoherence analysis. The study provides an important clinical application because most of studies based on EEG cross-bicoherence analysis have avoided the issue of VCUS. The cross-bicoherence analysis was performed by detecting the change in MSCB (Magnitude Square Cross-Bicoherence Function) between EEG activities of change detection and no-change detection trials. The real EEG signals were used which were recorded from 15 healthy subjects performing the visual modified delayed matching-to-sample paradigm experiment. The results obtained showed the significant effects of VCUS on the statistical analysis of the results for comparatively short inter-electrode spacing less than the 4cm.

Key Words: **EEG, Volume Conduction Effects, Nonlinear Signal Processing, Cross-Bicoherence Function.**

1. INTRODUCTION

EEG are electric potentials which are recorded from the brain. Literature discusses various clinical applications of EEG in the field of neurology [1-3]. Over the years, various signal processing techniques have been developed in order to study the EEG signals for different cognitive and neurological disorders. These signal processing techniques can be divided into linear and non-linear techniques. The coherence function is the linear signal processing method which reveals linear relationship between EEG signals in terms of their phase

* Assistant Professor, Institute of Physics, University of Sindh, Jamshoro.
* Professor, Institute of Physics, University of Sindh, Jamshoro.
*** Associate Professor, Institute of Business and Administration, University of Sindh, Jamshoro.

and amplitude [4]. It has been frequently used in EEG analysis to identify the functional relationship between EEG activities and therefore it has various clinical applications in neurology [5-8]. The major disadvantage of coherence analysis is that it does not reveal nonlinear relationship between signals and therefore it is not useful method for identifying the nonlinear relationship between EEG signals. Literature reports EEG signals of various neurological and cognitive disorders which show the nonlinear relationship [9-14]. The cross-bicoherence function is one of signal processing tools which reveals nonlinear relationship between EEG signals in terms of QPC (Quadratic Phase Coupling). Two signals are said to be quadratically phase coupled if, following relationship holds: $\omega_1+\omega_2=\omega_3$; $\varphi_1+\varphi_2=\varphi_3$, where $\omega_1,\omega_2,\omega_3$ are frequencies of signals having phases ϕ_1,ϕ_2,ϕ_3 respectively. The cross-bicoherence for a time series $x(t_1)$,and $y(t_2)$ whose Fourier transforms at three different frequencies ω_1,ω_2, and ω_3 are $X(w_1)$,$Y(w_1)$,and $Y(w_1+w_2)$ is given by the relation

$$C(\omega_1,\omega_2)=\frac{B^{xy}(\omega_1,\omega_2)}{\sqrt{P^x(\omega_1)P^y(\omega_1+\omega_2)}} \tag{1}$$

where $B^{xy}(\omega_1,\omega_2)=X(\omega_1)y(\omega_2)\,Y^*(\omega_1+\omega_2)$ is the cross-bispectrum and $P^x(\omega_1)=X(\omega_1)\,X^*(\omega_1)$ $P^y(\omega_2)=Y(\omega_2)\,Y^*(\omega_2)$ and $P^y(\omega_1+\omega_2)=Y(\omega_1+\omega_2)\,Y^*(\omega_1+\omega_2)$ are the power spectra at frequencies ω_1,ω_2,and ω_3 respectively. The Equation 1 is normalized cross-bispectrum whose larger and smaller values reveals strong and weak relationship between the three harmonic components. The literature reports various clinical applications of cross-bicoherence function in neurology. For example it has been used to study the levels of anesthesia [15-19], to understand the neurophysological mechanism of cognitive processes [20-22], to examine the changes in EEG patterns of full term newborns [23] and to examine the relationship between nonlinear interaction and seizure activity [11,24] and various other disorders [25-29].

The VCUS effects present in the brain can produce the biased estimates into the results of EEG bicoherence analysis by introducing the artificial bicoherence into its true value. There is some considerable literature regarding the VCUS effects [30-32], most of this work is based on the spherical models of the head in which various characteristics of VCUS on Fourier-based coherence have been discussed. Literature discusses some useful techniques for minimizing the VCUS effects on the Fourier-based coherence function, among them the most commonly and useful technique is based upon the SL (Scalp Laplacian) [33]. The SL is the second order spatial derivative of scalp potential which is the useful approximation of radial scalp current density. The radial scalp current density has the efficiency to minimize the activity generated by so neighboring sources and because of this SL-based coherence function has been found a useful tool for minimizing the VCUS effects. However SL-based coherence method does not replace the conventional EEG-based coherence method as an alternative tool for examining EEG signals. This is because SL-based coherence analysis provides suitable estimation when neighboring electrodes are present with at most inter-electrode spacing of 3.2cm. Even though various interpolation methods have been developed to address this issue, the artificial coherence due to the spline coefficients is major issue [4]. Therefore the use of both EEG and SL-based coherence methods is suitable for the comprehensive understanding of coherence analysis.

2. MAIN OBJECTIVES OF STUDY

As mentioned earlier that literature discusses VCUS effects on coherence function which is quite a different technique than cross-bicoherence function. The volume conduction effects on cross-bicoherence function have not been investigated to date to the best of our knowledge. Therefore this study investigates the VCUS present in the brain on cross-bicoherence function. A real EEG data and the simulated data to uncorrelated sources present in the brain, which was based upon the four-spherical shell model of head, were used in order to examine the effects of VCUS on cross-bicoherence function. Some important characteristics of VCUS effects on cross-bicoherence were investigated which can be proved useful in detecting biased estimates of cross-bicoherence function due to VCUS effects.

The next part of this study demonstrates the importance of minimizing the VCUS effects in the study of cross-bicoherence difference between EEG activities of change detection and no-change detection trials. This study has important clinical application, because most of studies based on comparing cross-bicoherence function of two different EEG activities have avoided the issue of VCUS. The real EEG signals were used which were recorded from healthy subjects performing the visual modified delayed matching-to-sample paradigm experiment. This study was performed as follows. The MSCB (Magnitude Square of Cross-Bicoherence) functions corresponding to real EEG of change detection and no-change detection trials were compared to each other. The difference in the EEG-based MSCB function was assessed using the Wilcoxon rank-sum test. The same study was repeated using the SL-based MSCB function. Finally statistical significance of both studies which were based on EEG-based MSCB and SL-based MSCB functions were compared for examining the VCUS effects on the statistical analysis of results.

3. METHODS

3.1 EEG Recording

The EEG for this study were recorded in the laboratory of the Centre for Cognition and Neuroimaging at Brunel University. The healthy group of 15 subjects was selected from the group of people who were recruited as paid volunteers through advertisements. The subjects were diagnosed from trained neurologist and General physician for any mental and physical disorder respectively and no sign of mentally and physically disorder was observed. The ages of subjects were between 16 and 25 years. The EEG recording was made for eliciting the ERP (Event Related Potentials) using 64 electrodes whose positions were adjusted on scalp according to extended 10-20 system of electrode's position. ERPs were recorded through modified delayed matching-to-sample paradigm experiment [34]. In this experiment, each subject was shown 18 pictures (called here stimuli) selected from the study of [35]. The subjects were shown pictures in three ways. In first condition, only single picture was shown to the subject. In second condition, two same pictures were shown to the subjects. And in third condition two different pictures were shown to the subjects. The subjects, who were sitting in front of computer screen, were instructed to press the mouse key if they were confident in recognizing the similarity or non-similarity. The trial was called hit trial if subjects were successful in recognizing the similarity or non-similarity otherwise it was called false trial. Each trial appeared with the time interval of 3.2 seconds and time duration between each picture in each trial was fixed to 1.6 seconds.

The sampling rate for converting ERPs into digital signal was set to 256Hz. The artifacts caused by the subjects as well as by the external sources were carefully minimized during the recording procedure. The subjects were asked to avoid any unnecessary movement of their body parts including their eyes. The bandpass filter of range 0.02-50Hz was also used for filtering out the low frequency artifacts of electrogalvanic signals and high frequency artifacts of electromyographic signals. The artifacts caused due to electromagnetic radiation were minimized by recording the ERPs in a sound attenuated radio frequency shielded room.

3.2 Simulation of EEG

EEG data was simulated using the following equations based on the 4 concentric sphere model of the head as described in [4].

$$\frac{V_{20}}{V_0} = 34.1e^{-0.15\theta} + 1.29 - 0.123\theta + 0.00164\theta^2 \qquad (2)$$

$$\frac{V_{40}}{V_0} = 27.4e^{-0.10\theta} - 5.49 + 0.203\theta - 0.00234\theta^2 \qquad (3)$$

$$\frac{V_{80}}{V_0} = 13.4e^{-0.10\theta} - 0.155 - 0.0135\theta \qquad (4)$$

where $\frac{V_{40}}{V_0} = \frac{1d}{4\pi\sigma R^2}$

The Equations (2-4) correspond to brain-to-skull conductivity ratio of σ_1/σ_3=20,40, and 80 respectively. The potentials V_{20}, V_{40}, V_{80} are normalized potentials with respect to the potential V_0. The scalp radius R of length 9cm and the current of 1μA flowing between poles of dipole length 1mm having the resistivity of 300 Ωcm was used in order to estimate V_0. The Equations (2-4) are derived for scalp conductivity equals to brain conductivity, and with csf (Cerebrospinal Fluid) conductivity equals to five times the brain conductivity. The radial distances of skull surface, cerebral spinal fluid layer, brain surface, dipole EEG source are assumed 8.5, 8,7.9, 7.8 cm respectively. The angle q is defined for the interval of [0,50°].

3.3. Estimation of the Scalp Laplacian

The techniques for estimating the SL can be divided into local [33,37-38] and global methods [39-40]. In local methods , the SL at electrode position X_o is approximated by the scalp potentials recorded from the nearest positions to the electrode position X_o. The Equation (2) outlines the method for estimating the SL using one of the local methods. The global methods are based on various interpolation techniques and they are suitable when neighboring electrodes are not available. However global methods produce artificially high coherence due to the coefficients of spline. The SL was estimated using both the local method based on Hjorth method [33] and the global method based on Perrin method [39]. The local method comparatively provided better value of SL. Its characteristics as mentioned in the literature were more close to the real value of the SL as compared to the one estimated using global method. The global method based SL produced interpolation noise. Therefore Hjorth method was selected for further analysis and it was estimated using the following relation:

$$I(t) = x(t) - \frac{x_1(t) = x_2(t) + x_3(t)x_4(t)}{4} \qquad (5)$$

where $x_1(t)$, $x_2(t)$, $x_3(t)$,and $x_4(t)$ are scalp potentials recorded at electrodes which are nearest neighbors to the position of electrode where scalp potential x(t) is measured.

3.4 Estimation of cross-bicoherence

The cross-bicoherence is non-linear signal processing method which measures the relationship between three frequency components in terms of QPC. The cross-bicoherence of two EEG time series x(t) and y(t) and their corresponding SLs $I_x(t)$ and $I_y(t)$ respectively were estimated following the method of [36] which is based upon average cross bicoherence across all repeated trials. Let $x_n(t_1)$ and $y_n(t_2)$ be the single trial time series whose fast Fourier transforms at two different frequencies are $X_n(\omega_1)$ and $Y_n(\omega_2)$ respectively. The cross-bicoherence was computed using the following relation:

$$\frac{\Sigma_{n-1}^{n=m} B_n^{xy}(\omega_1,\omega_2)}{\sqrt{P_n^x(\omega_1), P_n^y(\omega_2) P_n^y(\omega_1+\omega_2)}} \qquad (6)$$

Equation (2) outlines the procedure for estimating the cross-bicoherence function. Let $[x_1(t_1), x_2(t_1), x_3(t_1)\ldots x_m(t_1)]$ and $[y_1(t_1), y_2(t_1), y_3(t_1)\ldots y_m(t_1)]$ be the series of repeated trials whose corresponding fast Fourier transforms are $[X_1(\omega_1), X_2(\omega_1), X_3(\omega_1)\ldots X_m(\omega_1)]$ and

$[Y_1(\omega_1), Y_2(\omega_1), Y_3(\omega_1)\ldots Y_m(\omega_1)]$ respectively. The cross-bicoherence for each trial is $B_n^x y(\omega_1,\omega_2)=X_n(\omega_1)\, Y_n(\omega_1)\, Y_n^*(\omega_1+\omega_2)$. The power spectra of two time series at three frequencies ω_1, ω_2,and $\omega_1+\omega_2$ in each trial are $P_n^x(\omega_1)=X_n(\omega_1)\, X_n^*(\omega_1)$, $P_n^y(\omega_2)=Y_n(\omega_2)\, Y_n^*(\omega_2)$, and $P_n^y(\omega_1+\omega_2)=Y_n(\omega_2)\, Y_n^*(\omega_2)$ respectively. After estimating the average of cross-bispectra and power spectral densities across repeated trials, the estimates for cross and auto spectra and they lead to the estimate of cross-bicoherence as expressed in Equation (2). The The magnitude square of cross-bicoherence which is abbreviated as MSCB is estimated by taking the square of the absolute value of Equation (2).

3.5 Statistical Analysis

The estimation of the cross-bicoherence using a number of repeated trials has a bias and variance and therefore it is important to examine whether the estimated value of is statistically significant or not. The statistical significance of cross-bicoherence was assessed by the following relation [41]:

$$T(\omega_1,\omega_2) > \frac{2e}{\sqrt{m}} \tag{7}$$

Where *m* represents the number of repeated trails. The error *e* is estimated by the relation:

$$\varepsilon\left[C(\omega_1,\omega_2)\right] = \left(\frac{C(\omega_1,\omega_2)}{\omega_1^{\max}\omega_2^{\max}\left(\omega_1^{\max}+\omega_2^{\max}\right)m}\right)^{\frac{1}{2}} \tag{8}$$

where ω_1^{max}, and ω_1^{max} are maximum values of frequencies. The statistical significance was set to 95% and any value less than $\frac{2e}{\sqrt{m}}$ was rejected.. The non-parametric Wilcoxon rank-sum test was applied in order to examine the cross-bicoherence difference between EEG activities of change detection and no-change detection trials. The p-value of 0.05 was considered as the significant level.

4. RESULTS AND DISCUSSION

Positions of electrodes on various regions of the brain are shown in Fig. 1. The VCUS effects on cross-bicoherence were analyzed using the simulated data generated due to uncorrelated brain sources. In order o assess the effects of inter-electrode spacing on MSCB function due to VCUS, the average of MSCB was taken across frequencies w_1 and w_2. The average MSCB function was then examined between electrode X and rest of the electrodes on the scalp. The results were examined using the topographic maps. The larger MSCB function was examined for short inter-electrode spacing and it gradually decreased as inter-electrode spacing increased. The topographic maps as shown in Fig. 2 were proved to useful tool in examining the effects of inter-electrode space on the average MSCB function due to VCUS. For example Fig. 3 shows one of the topographic maps in which average MSCB function due to VCUS effects between electrodes CPZ and rest of the electrodes on scalp is shown. Fig. 2 clearly indicates that intensity of average MSCB function decreases as the inter-electrode spacing between electrode CPZ and other electrodes increases. The average MSCB function is larger in intensity for electrodes which are nearest neighborhood to the electrode CPZ. However this intensity tends to decreases as the inter-electrode spacing increases. The MSCB function due to VCUS effects was also found dependant on the angular distance of electrode's position. This is because a gradual decrease in MSCB function as a function of inter-electrode spacing was observed only for increase in inter-electrode spacing in fixed direction otherwise the results were not consist. Several values of MSCB function were observed which showed either increase or decrease in values for inter-electrode spacing which was increased in different directions rather than in some fixed direction.

The effects of frequencies w_1 and w_2 were also examined. The MSCB function due to VCUS was found independent of both frequencies w_1 and w_2. This result is illustrated in

Fig. 3 in which MSCB between two nearest pair of electrodes C_1 and C_3 is shown. The values of MSCB function due to the VCUS effects is large because of larger VCUS effects due to minimum inter-electrode spacing. However, it is clear in Fig. 3 that MSCB is almost constant in frequency domain of ω_1 and ω_2. The SL-based MSCB values were found almost zero as compared to the values of corresponding EEG based MSCB function which provides an evidence that SL-based MSCB function minimizes the effects of VCUS effects.

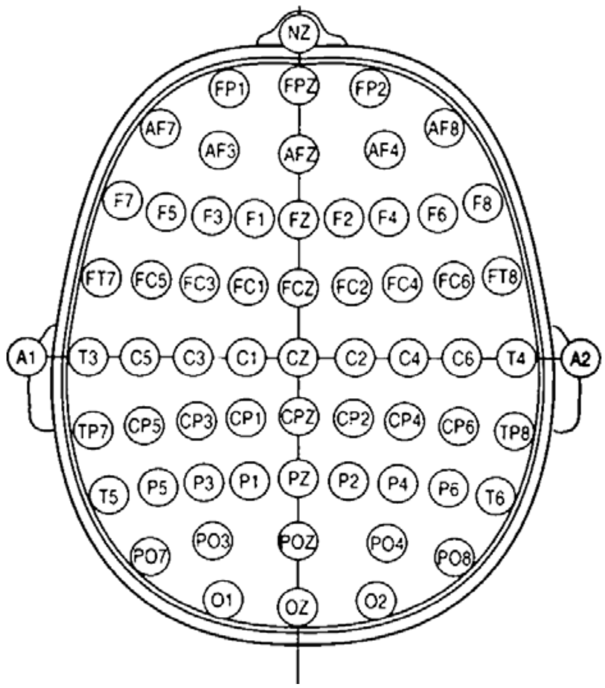

FIG. 1. POSITION OF ELECTRODES BASED ON EXTENDED 10-20 SYSTEM

The results of next part of study are discussed below which was based on examining the VCUS effects on the difference in MSCB function between EEG activities of change detection and no-change detection trials. The most of real EEG-based MSCB spectra for comparatively smaller inter-electrode spacing was found independent of both frequencies w_1 and w_2 and it was showing gradual decrease with the increase in inter-electrode spacing. This leads to the conclusion that such MSCB spectra were affected by VCUS effects because it was shown previously in this study that EEG-based MSCB function due to VCUS effects does not change with frequencies w_1 and w_2 and depends

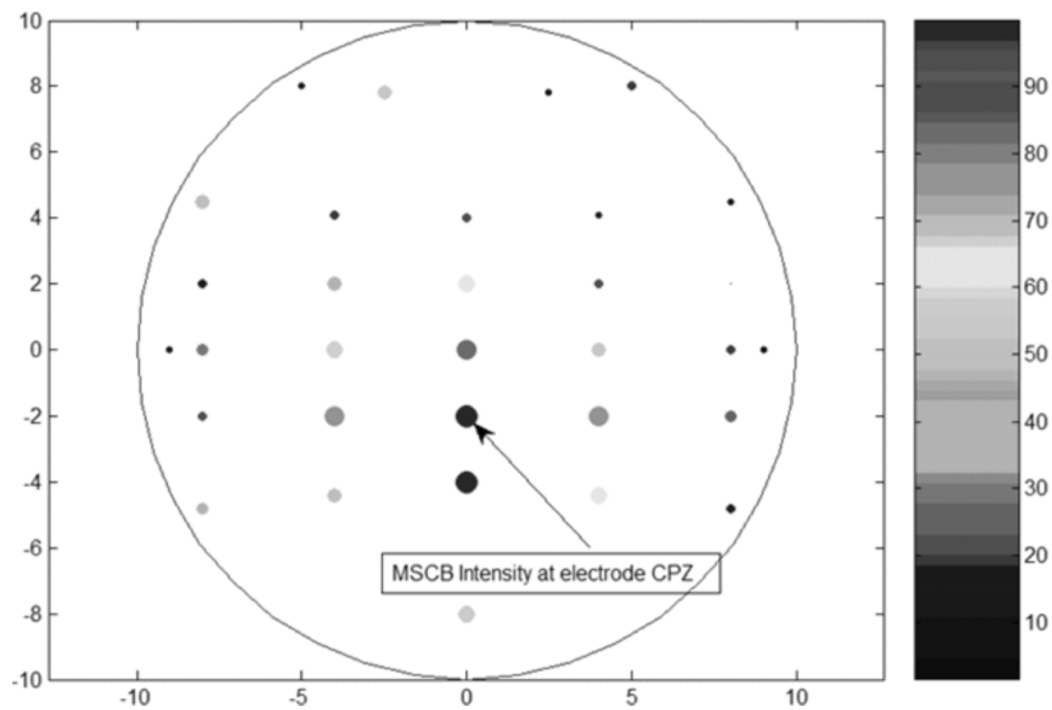

FIG. 2. THE INTENSITY OF MSCB FUNCTION BETWEEN ELECTRODE CPZ AND REST OF ELECTRODES THE INTENSITY IS LARGER FOR THE NEAREST ELECTRODES TO CPZ AND FOR LARGER DISTANCE THE INTENSITY OF CPZ IS COMPARATIVELY LOW IN VALUE

upon the inter-electrode spacing. On the other hand corresponding SL-based MSCB spectra showed dependence on both frequencies w_1 and w_2 which provides the evidence that SL-based MSCB has the ability to minimize the VCUS effects. The Tables 1-2 show the difference of EEG and SL-based average MSCB functions (across all subjects) between corresponding change detection and no-change detection trials with the score of Wilcoxon rank-sum test for inter-electrode spacing of larger than 7cm and for inter-electrode spacing of less than 4cm respectively. As shown in these tables that both SL and EEG-based average MSCB functions exhibit larger value for change detection trial as compared to those for no-change detection trials. However, the Wilcoxon rank-sum test could not reveal any statistically significant difference between average MSCB functions of change detection and no-change detection trials. The noticeable change into the level of statistical significance due to VCUS effects was observed for both SL and EEG-based MSCB analysis which is discussed as.

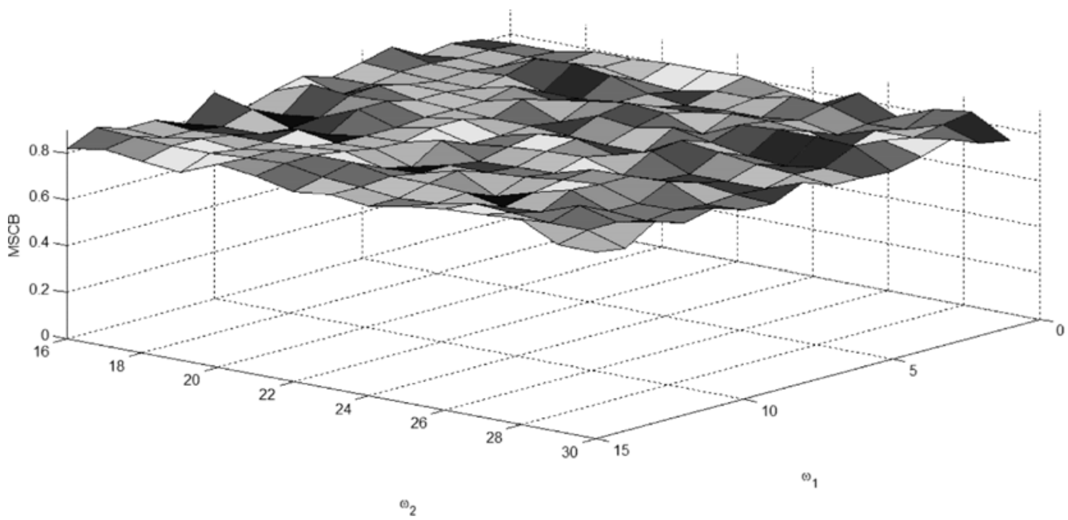

FIG. 3. THE MSCB FUNCTION DUE TO VCUS SOURCES IS ALMOST CONSTANT AT ω_1 AND ω_2 FREQUENCIES

TABLE 1. THE DIFFERENCE IN MSCS BETWEEN MATCHING AND NON-MATCHING TRIALS FOR INTER-ELECTRODESPACING LARGER THAN 7CM

MSCB Method		F1-F6	F3-F4	F2-F5	P1-P6	P4-P5	P6-P3	P
EEG-Based	MT	0.60	0.67	0.61	0.78	0.43	0.53	0.40
	NMT	0.48	0.56	0.73	0.70	0.31	0. 41	
SL-Based	MT	0.61	0. 65	0.52	0.70	0.41	0.51	0.39
	NMT	0.50	0.59	0.69	0.52	0.30	0.42	

TABLE 2. THE DIFFERENCE IN MSCS BETWEEN MATCHING AND NON-MATCHING TRIALS FOR INTER ELECTRODE SPACING LESS THAN 4CM

MSCB Method		F1-F6	F3-F4	F2-F5	P1-P6	P4-P5	P6-P3	P
EEG-Based	MT	0.71	0.90	0.82	0.51	0.83	0.88	0.20
	NMT	0.40	0.62	0.52	0.73	0.91	0.61	
SL-Based	MT	0.50	0.72	0.61	0.30	0.61	0.73	0.31
	NMT	0.31	0.50	0.39	0.51	0.74	0.50	

As shown in Table 2 that for inter-electrode spacing of less than 4cm, the EEG based MSCB analysis reveled larger statistical significance as compared to the one corresponding to the SL-based MSCB analysis. Such increase in statistical significance in EEG-based MSCB analysis is due to the presence of VCUS effects. This justification results due to the fact that most of EG-based MSCB spectra for inter-electrode spacing of less than 4cm were found affected by VCUS effects whereas corresponding SL-based MSCB spectra were found close to a true MSCB spectra. For inter-electrode spacing larger than 7cm, the spectra of both SL and EEG-based MSCB functions were found qualitatively close to the true MSCB spectra. And because of this as shown in Table 1 that both SL and EEG-based MSCB methods exhibit smaller difference in p-value. The MSCB spectra obtained using the inter-electrode spacing of larger than 7cm shows comparatively very less effects of VCUS on the results of study based on difference of MSCB function between change detection and no-change detection trials. However, this study examines significant effects of VCUS on the results of same study corresponding to the inter-electrode spacing of less than 4cm. It can be concluded that VCUS effects are not additive and therefore can not be separated by comparing two or more than two EEG-based MSCB functions of two different EEG activities . However VCUS effects produce less effects on the results of MSCB difference if the inter-electrode spacing is large enough otherwise results can be significantly biased by the VCUS effects.

5. CONCLUSION

This study is divided into two main parts. The first part presents the important findings regarding the characteristics of VCUS on EEG-based MSCB function. These findings can be proved useful tool for detecting the biased estimates of MSCB function due to VCUS in EEG-based MSCB analysis. The second part is based upon examining the effects of VCUS on statistical analysis of MSCB difference between change detection and no-change detection trials. The results showed that VCUS effects might introduce the significant biased estimates into the results of such study if the inter-electrode spacing is less than 4cm. However VCUS effects showed minor effects on the results of study for inter-electrode spacing of larger than 7cm. The results of this study put a question mark on several MSCB studies which are based upon smaller inter-electrode spacing and in which VCUS effects have not been minimized while comparing the EEG-based MSCB function between two or more than two different EEG activities.

ACKNOWLEDGEMENT

The authors thank to Centre for Cognition and Neuroimaging, Brunel University, UK, for allowing them to record EEG data.

REFERENCES

[1] Kennedy, J.D., and Gerard, E.E., "Continuous EEG Monitoring in the Intensive Care Unit", Current Neurology and Neuroscience Reports, Volume 12, No. 4, pp. 419-428, 2012.

[2] Loo, S.K., and Makeig, S., "Clinical Utility of EEG in Attention-Deficit/Hyperactivity Disorder: A Research Update", Neurotherapeutics, Article in Press, 2012.

[3] Michel, C.M., and Murray, M.M., "Towards the Utilization of EEG as a Brain Imaging Tool", NeuroImage, Volume 61, No. 2, pp. 371-385, 2012.

[4] Nunez, P ., "Electric Fields of the Brain", 1st Edition, Oxford Press, New York, USA, 1981.

[5] Sherman, D.L., Tsai, Y.C., Rossell, L.A., Mirski, M.A., and Thakor, N.V., "Spectral Analysis of a Thalamus-to-Cortex Seizure Pathway", IEEE Transactions on Biomedical Engineering, Volume 44, No. 8, pp. 657-664, 1997.

[6] Winterer, G., Enoch, M.A., White, K.V., Saylan, M., Coppola, R., and Goldman, D., "EEG Phenotype in Alcoholism: Increased Coherence in the Depressive Subtype", Acta Psychiatrica Scandinavica, Volume 108, No. 1, pp. 51-60, 2003.

[7] Weiss, S., and Mueller, H.M., "The Contribution of EEG Coherence to the Investigation of Language", Brain and Language, Volume 85, pp. 325-343, 2003.

[8] Hoffman, R.E., Buchsbaum, M.S., Escobar, M.D., and Makuch, R.W., Nuechterlein, K.H., Guich, S.M., "EEG Coherence of Prefrontal Areas in Normal and Schizophrenic Males During Perceptual Activation", Journal of Neuropsychiatry and Clinical Neuroscience, Volume 3, No. 2, pp. 169-175, 1991.

[9] Breakspear, M., and Terry, J.R., "Detection and Description of Non-Linear Interdependence in Normal Multichannel Human EEG Data", Clinical Neurophysiology, Volume 113, No. 5, pp. 735-753, 2002.

[10] Liu, Z., Rios, C., Zhang, N., Yang, L., Chen, W., and He, B., "Linear and Nonlinear Relationships between Visual Stimuli, EEG and Bold FMRI signals", NeuroImage, Volume 50, No. 3, pp. 1054-1066, 2010.

[11] Sherman, D., Zhang, N., Garg, S., Thakor, N.V., Mirski, M.A., White, M.A., and Hinich, M.J., "Detection of Nonlinear Interactions of EEG alpha Waves in the Brain by a New Coherence Measure and its Application to Epilepsy and Anti-Epileptic Drug Therapy", International Journal of Neural Systems, Volume 21, No. 2, pp. 115-126, 2011.

[12] Carlino, E., Sigaudo, M., Pollo, A., Benedetti, F., Mongini, T., Castagna, F., Vighetti, S. and Rocca, P., "Nonlinear Analysis of Electroencephalogram at Rest and during Cognitive Tasks in Patients with Schizophrenia", Journal of Psychiatry and Neuroscience, Volume 37, No. 4, pp. 259-266, 2012.

[13] Pradhan, C., Jena, S.K., Nadar, S.R., and Pradhan, N., "Higher-Order Spectrum in Understanding Nonlinearity in EEG Rhythms", Computational and Mathematical Methods in Medicine, Volume 12, pp. 206857, 2012.

[14] Yuan, Q., Zhou, W., Liu, Y. and Wang, J., "Epileptic Seizure Detection with Linear and Nonlinear Features", Epilepsy and Behavior, Volume 24, No. 4, pp. 415-421, 2012.

[15] Hayashi, K., Sawa, T., and Matsuura, M., "Anesthesia Depth-Dependent Features of Electroencephalographic Bicoherence Spectrum during Sevoflurane Anesthesia", Anesthesiology, Volume 108, No. 5, pp. 841-850, 2008.

[16] Pritchett, S., Zilberg, E., Xu, Z.M., Myles, P., Brown, I., and Burton, D., "Peak and Averaged Bicoherence for Different EEG Patterns during General Anaesthesia", Biomedical Engineering Online, Volume 9, pp. 76, 2010.

[17] Morimoto, Y., Hagihira, S., Yamashita, S., Iida, Y., Matsumoto, M., Tsuruta, S., and Sakabe, T., "Changes in Electroencephalographic Bicoherence During Sevoflurane Anesthesia Combined with Intravenous Fentanyl", Anesthesia and Analgesia, Volume 103, No. 3, pp. 641-645, 2006.

[18] Mukamel, E.A., Wong, K.F., Prerau, M.J., Brown, E.N., and Purdon, P.L., "Phase-Based Measures of Cross-Frequency Coupling in Brain Electrical Dynamics under General Anesthesia", Proceedings Annual International Conference of the IEEE Engineering in Medicine and Biology Society, pp. 1981-1984, 2011.

[19] Pritchett, S., Zilberg, E., Xu, Z.M., Myles, P., Brown, I., and Burton, D., "Peak and Averaged Bicoherence for Different EEG Patterns During General Anaesthesia", Biomedical Engineering Online, Volume 9, pp. 76, 2010.

[20] Isler, J.R., Grieve, P.G., Czernochowski, D., Stark, R.I., and Friedman, D., "Cross-Frequency Phase Coupling of Brain Rhythms During the Orienting Response", Brain Research, Volume 32, No. 12, pp. 163-172, 2008.

[21] Schack, B., Rappelsberger, P., Vath, N., Weiss, S., Moller, E., Griessbach, G., and Witte, H., "EEG Frequency and Phase Coupling During Human Information Processing", Methods of Information in Medicine, Volume 40, No. 2, pp. 106-111, 2001.

[22] Schack, B., Vath, N., Petsche, H., Geissler, H.G., and Moller, E., "Phase-Coupling of Theta-Gamma EEG Rhythms During Short-Term Memory Processing", International Journal of Psychophysiology, Volume 44, No. 2, pp. 143-163, 2002.

[23] Witte, H., Putsche, P., Schwab, K., Eiselt, M., Helbig, M., and Suesse, T., "On the Spatio-Temporal Organisation of Quadratic Phase-Couplings in Trace Alternant EEG Pattern in Full-term Newborns", Clinical Neurophysiology, Volume 115, No. 10, pp. 2308-2315, 2004.

[24] Villa, A.E., and Tetko, I.V., "Cross-Frequency Coupling in Mesiotemporal EEG Recordings of Epileptic Patients", Journal of Physiology, Volume 104, No. 3, pp. 197-202, 2010.

[25] Bullock, T.H., Achimowicz, J.Z., Duckrow, R.B., Spencer, S.S., and Iragui-Madoz, V.J., "Bicoherence of Intracranial EEG in Sleep, Wakefulness and Seizures", Electroencephalography and Clinical Neurophysiology, Volume 103, No. 6, pp. 661-678, 1997.

[26] Chua, K.C., Chandran, V., Acharya, U.R., and Lim, C.M., "Application of Higher Order Statistics/Spectra in Biomedical Signals", Medical Engineering and Physics, Volume 32, No. 7, pp. 679-689, 2010.

[27] Diamond, P.H., Rosenbluth, M.N., Sanchez, E., Hidalgo, C., Van Milligen, B., Estrada, T., Branas, B., Hirsch, M., Hartfuss, H.J., and Carreras, B.A., "In Search of the Elusive Zonal Flow Using Cross-Bicoherence Analysis", Physical Review Letters, Volume 84, No. 21, pp. 4842-4845, 2000.

[28] Huang, L., Zhao, J., Singare, S., Wang, J., and Wang, Y., "Discrimination of Cerebral Ischemic States Using Bispectrum Analysis of EEG and Artificial Neural Network", Medical Engineering and Physics, Volume 29, No. 1, pp. 1-7, 2007.

[29] Siu, K.L., and Chon, K.H., "On the Efficacy of the Combined Use of the Cross-Bicoherence with Surrogate Data Technique to Statistically Quantify the Presence of Nonlinear Interactions", Annals of Biomedical Engineering, Volume 37, No. 9, pp. 1839-1848, 2009.

[30] Nunez, P ., "Electric Fields of The Brain", 1st Edition, Oxford Press, New York, USA, 1981.

[31] Srinivasan, R., Nunez, P.L., and Silberstein, R.B., "Spatial Filtering And Neocortical Dynamics: Estimates of EEG Coherence", IEEE Transactions on Biomedical Engineering, Volume 45, No. 7, pp. 814-826, 1998.

[32] Srinivasan, R., "Methods to Improve the Spatial Resolution of EEG", International journal of Bioelectromagnetism, Volume 1, pp. 102-111, 1999.

[33] Hjorth, B., "An Online Transformation of EEG Scalp Potential into Orthogonal Source Derivation", Electroencephalography and Clinical Neurophysiology, Volume 39, pp. 526-530, 1975.

[34] Zhang, X.L., Begleiter, H., Porjesz, B., and Wang, W., "Event Related Potentials During Object Recognition Tasks", Brain Research Bulletin Volume 38, pp. 531-538, 1995.

[35] Snodgrss, J.G., and Vanderwart, M., "A Standardized Set of 260 Pictures: Norms for the Naming Agreement, Familiarity, and Visual Complexity", Journal of Experimental Psychology: Human Learning and Memory, Volume 6, pp. 174-215, 1980.

[36] Nikias, L.C., and Petropulu, A.P., "Higher-Order Spectra Analysis", PTR Prentice Hall, Englewood Cliffs, New Jersey, USA, 1993.

[37] Katznelson, R., "EEG Recordings, Electrode Placement, and Aspects of Generator Localization". In PL Nunez, Electric Fields of the Brain: the Neurophysics of EEG, pp. 176-213, Oxford University Press, New York, USA, 1981.

[38] Gevins, A.S., Brickett, L.E., Reutter, P., and Desmond, J., "Seeing Through the Skull: Advanced EEGs Use to Accurately Measure Cortical Activity from the Scalp", Brain Topography, Volume 4, No. 2, pp. 125-131, 1991.

[39] Perrin, F., Bertrand, O., and Pernier, J., "Scalp Current Density Mapping: Value and Estimation from Potential Data", IEEE Transactions on Biomedical Engineering, Volume 34, No. 4, pp. 283-288, 1987.

[40] Pernier, J., Perrin, F., and Bertrand, O., "Scalp Current Density Fields: Concepts and Properties", Electroencephalography and Clinical Neurophysiology, Volume 69, pp. 385-389, 1988.

[41] Shils, J.L., Litt, M., Skolnick, B.E., and Stecker, M.M., "Bispectral Analysis of Visual Interactions in Humans", Electroencephalography and Clinical Neurophysiology, Volume 98, pp. 113-125, 1996.